

Advance directives for non-therapeutic dementia research: some ethical and policy considerations

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Abstract

This paper explores the use of advance directives in clinical dementia research. The focus is on advance consent to participation of demented patients in non-therapeutic research involving more than minimal risks and/or burdens.

First, morally relevant differences between advance directives for treatment and care, and advance directives for dementia research are discussed. Then attention is paid to the philosophical issue of dementia and personal identity, and the implications for the moral authority of research advance directives. Thirdly, a number of practical shortcomings of advance directives for non-therapeutic dementia research are explored and attention is paid to the role of proxies.

It is concluded that upon a closer look the initial attractiveness of advance directives for dementia research is lessened, and that it is doubtful whether these instruments can compensate for the lack of subject consent in case of non-therapeutic dementia research involving more than minimal risks and/or burdens for the incompetent demented subject.
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"...the obsessed curiosity in our nature, spilling her time by anticipating future matters, as if it is not sufficient to cope with present matters..."

Michel de Montaigne, Essays

Introduction

Advance care documents, which include advance directives, living wills, and durable powers of attorney, have recently become popular tools, because it is widely held that they enable patients to exercise greater control over treatment decisions in case of future incompetence. Advance directives are instruments which express precedent autonomy in order to promote the autonomy-interests of patients who may become incompetent and thus unable to express their wishes and preferences with regard to treatment and care.¹

In general, advance directives regarding future treatment decisions are negatively formulated, in the sense that they contain a specified refusal of treatment (for instance in the case of irreversible coma/persistent vegetative state {PVS} or severe dementia). Apart from hard cases (ie if the directive is unclear or if statements are contradictory), such advance directives, from a moral and legal viewpoint, ought to be respected by physicians. It should be noted, however, that in cases of dementia, advance directives may bring with them particular problems regarding interpretation and implementation.²

Although originally developed in the context of care and treatment decision-making, recently, in practice and in the literature, interest has grown in the use of advance directives in the context of medical research, particularly research involving cognitively impaired persons.³⁻⁸ Potential candidates for the drafting of such advance directives for research include individuals in the earliest stages of progressive dementia and those experiencing intermittent incompetency due to mental disorder. Advocates of this approach contend that the use of research advance directives furthers respect for persons by creating a new opportunity for persons to exercise autonomous choice.⁹ This paper focuses on clinical dementia research.

The increasing interest in advance directives for dementia research is the result of several factors and developments. Firstly, there is a scientific need to conduct research into dementia for which it is necessary to involve demented patients who are in the later and more severe stages of the disease process. Secondly, given the importance of informed consent as a prerequisite for the conduct of scientific research with human beings, and given the fact that patients suffering from dementia, particularly in the later stages of the illness, generally will lack the ability to make informed decisions, advance directives for research especially in the area of dementia are attractive. Advance consent for research in case of incompetence may be a substitute for the lack of informed

consent of the incompetent demented subject. A third factor of relevance is that as the interest in dementia research is growing, so also is the need to remove possible obstacles to dementia research. The debate in society with regard to the acceptability of involvement of decisionally incapacitated humans (ie young children, the mentally handicapped and dementing patients) in research which has no reasonable prospect of benefiting these research subjects themselves (but may generate knowledge that may be of profit to future patients) - so-called non-therapeutic research - has led to an ethical consensus that this may be justified under specific conditions. One of these conditions is that such research may not involve more than minimal risks or burdens to the participating subject.¹⁰ Thus while there seems to be - or at least it seems there may be emerging - some legal space for conducting non-therapeutic research with demented patients who cannot give informed consent themselves, this space is certainly quite limited. The use of research advance directives might enlarge - at least theoretically - this restricted space.

Proponents view advance directives for dementia research as instruments that may bring about a reconciliation between two potentially conflicting goals: on the one hand the maintenance of adequate protection of vulnerable subjects suffering from dementia as subjects in scientific research, and on the other hand the societal goal of promoting scientific progress by conducting research involving incompetent demented subjects with possible future preventive, diagnostic and therapeutic benefits.¹¹

In this paper, I will focus on the possibilities and problems regarding the use of advance directives connected to *research involving more than minimal risk and/or burdens to the participating incompetent subject, with no prospect of direct benefit to him/her*. It is within the context of this type of research that advance directives might involve promises because, as mentioned, it is agreed that the involvement of incompetent human subjects in non-therapeutic research without their informed consent is not justified if the research is considered to involve more than minimal risks and burdens to the subject. Future-oriented consent in an advance directive might compensate for the lack of actual consent.

"Minimal risk" (in the definition adopted by the US Food and Drug Administration {FDA}) means that the risks of harm anticipated in a research project are not greater, considering probability and magnitude, than "those ordinarily encountered in daily life or during the performance of routine physical or psychological examina-

tions or tests".¹² In the research ethics literature one level higher than this critical threshold is "minor increment over minimal risk". The next level is "more than minor increment over minimal risk".

Non-therapeutic dementia research projects, if evaluated on the basis of the FDA definition of minimal risk, can be considered to involve a minor or even more than minor increment over minimal risk if for instance non-routine invasive procedures are applied. Lumbar punctures and positron emission tomography (PET) scans are examples of procedures that can be reasonably viewed as having greater than minimal risk for persons with dementia because 1. both procedures are invasive, 2. both carry the risk of pain and discomfort during and after, and 3. complications from either procedure can require surgery to correct.⁴

Before addressing one important moral question and some practical issues which are involved, attention will be paid to the differences between advance directives in the context of dementia care, and dementia research.

Differences between clinical advance directives and dementia research advance directives

As already mentioned, advance directives, historically, were introduced as instruments aiming at influencing medical treatment and care in case of future incompetence. Only recently have advance directives become the subject of debate in the context of research. Before discussing the morality of using advance directives for dementia research purposes, it may be helpful to look at possible morally relevant differences between advance directives for treatment and care on the one hand, and advance directives for dementia research on the other hand. Without trying to be exhaustive, three differences are important.

1. Most people who issue a care advance directive are motivated by fears of being medically overtreated if they end up in a state of incompetence. In the advance directive they generally describe in what situation they do not want treatment to be started or want treatment to be discontinued. This is a powerful factor motivating at least a number of people to execute formal advance directives. There is no parallel motivating factor for formal advance directives for dementia research.⁸ On the contrary, in the case of completing an advance directive for participation in non-therapeutic research, motivating reasons will have to be altruistic, and not self-interested.
2. In general, advance directives for treatment and care are executed when people are competent and

have the capacity to think about and imagine their future, and possible medical choices to be made in that future. In the case of dementia research advance directives, however, by the time patients with dementia are brought to medical attention, many are already impaired to the extent that they are unable to execute any kind of detailed advance directive for research.⁸

3. Clinical advance directives, in which generally a refusal of treatment in specified circumstances is described, have a stronger moral and legal force than research advance directives. This is so because the negative rights to privacy, bodily integrity and self determination (as evidenced by laws on assault and battery) lay stronger claims on others than the positive willingness to be a potential subject in scientific research. Moreover, in practical terms, it is much easier to formulate a statement refusing consent to treatment than to formulate one giving consent for research participation. The former can be framed in general terms (for example, a refusal of all life-saving interventions), whereas the latter has to be framed with reference to the particular intervention(s). Given that, by its nature, research is innovative, it would be very difficult to give advance consent for participation in a future experiment when one does not know, in advance, the nature of the experiment.

Given these differences between care advance directives and dementia research advance directives, it is obvious that moral, legal and practical questions with regard to the use of research advance directives deserve separate attention.

Dementia and personal identity

I now turn to a central moral problem in connection with advance directives for non-therapeutic research involving more than minimal burdens and/or risks to the incompetent demented subject. A philosophical issue which may seriously jeopardise the moral status of such advance directives is the question of the relationship between dementia and personal identity.

When people become demented, their self and personal identity are subject to more or less deep psychological changes. During the process of becoming demented, these changes may become so profound that the former person is no longer recognised by intimate others such as the spouse or children. The demented person often has little memory, or only fragmented memories, of her previous life, her personality has changed, her intellect has deteriorated, and she may have considerably different needs, concerns, beliefs,

and desires than before she became demented. Much of the psychological continuity which is often thought to be necessary for personal identity can be lost.¹³

This state of affairs raises the philosophical question of how we should view the relationship between the former and later selves of the person who suffers from dementia¹⁴ and whether personal identity can survive the process of dementia.

Two possible perspectives

Two general responses to this question can be distinguished. The first response is based on the view defended by Ronald Dworkin.^{1 15 16} Dworkin distinguishes between two possible perspectives that can be taken towards a dementing person. One may view a demented person as someone who *is* demented, or, alternatively, as someone who *has become* demented.¹⁵⁻¹⁶ If we look at the demented person as someone who *is* demented, then we focus on the actual situation and interests of that person. But if on the other hand we look at the demented person as someone who *has become demented*, then we take into consideration that dementia takes place in the course of the whole life of that person. Dworkin argues that we ought to take this latter perspective towards the dementing person. This perspective presupposes that the competent and demented stages in someone's life are phases within one single life, and that the competent and demented selves of the individual are part of the same person. The person whose rights we must consider is the whole person, the person who has led that full life through its various stages, and though the question of what rights he now has is affected, in various ways, by the stage he is now in, it is also affected by interests and concerns that transcend that stage and embrace his life as a whole.¹⁶ On Dworkin's account, a person may have so-called critical interests that have a stronger moral force than so-called experiential interests. A person's critical interests are the hopes and aims that lend genuine meaning and coherence to her life. Critical interests refer to the ideal of integrity, seeking to create a coherent narrative structure for the lives people lead.¹⁷

Experiential interests are connected to the value people attach to having specific experiences as an essential part of the good life. The value of these experiences depends on the fact that we do find them pleasurable or exciting as *experiences*.¹

Critical interests are judged by Dworkin as more important because they represent critical judgments rather than just experiential preferences.¹ Dworkin's account leads to the conclusion that advance consent and advance

directives ought to be respected because they are to be viewed as expressions of the critical interests a person has.

An alternative view with regard to dementia and personal identity is connected to the name of Derek Parfit.¹⁴

Parfit takes the view that psychological connectedness and continuity between the different stages in the life of a person may decrease and that this decrease of connectedness can diminish the force of commitments. In a metaphorical sense in the case of deep psychological changes between the former and later self of a dementing person one could say that these are different persons.

The implications of this view for the moral force and authority of advance directives have been framed in terms of a "slavery argument".¹⁸ This argument contains two premises that lead to a conclusion. The first premise is that an advance directive of one person has no moral force at all with regard to what needs to happen to another person. The second premise is that in certain cases of severe and permanent neurological damage the psychological continuity is so deeply disturbed that one may speak of another person. The conclusion then is that in those particular cases of neurological damage an advance directive issued by the former person has no moral force in connection to the course of action to be taken towards the person existing after neurological damage.

An important implication of Parfit's account is that the demented individual may have separate interests as a demented individual which are to be distinguished from the interests of the former competent self of that individual.

I will not try to resolve this philosophical debate about the relationship between dementia and personal identity. Nevertheless, in connection with the issue of advance directives for dementia research, in my view, the following observations have relevance and importance.

Moral authority

Firstly, if Parfit's position has any moral force - which in my view it cannot be denied - then it seems to me that it at least questions the moral authority of advance directives for dementia research as well as the moral authority of advance directives for dementia treatment and care.^{9 17} It raises doubt about the unconditional moral authority of the former self to decide what can happen to the later demented self, be it in the context of research or in the context of treatment and care.

A second observation concerns the "distance" between the former and later self of the demented

individual. If the memory loss and other psychological changes accompanying the dementia process become more severe, then the binding force of the formerly expressed wishes becomes weaker. This would imply that the moral authority of a research advance directive would be less diminished in case of conducting research in the earlier phases of dementia than in the later and more severe stages of dementia. This arguably also applies to advance directives for treatment and care.

A third observation is that if we take the Dworkin position seriously, this implies that in the final analysis we ought to accept and defend subjecting a refusing or resisting demented patient to research interventions for which the former competent self has given consent in advance, because doing this would be in his or her critical interests. In the words of one of the critics of Dworkin we might say that here an elegant theory may lead to a questionable policy.¹⁷

Practical problems and shortcomings of advance directives for dementia research

As well as the moral problems that have been identified, there are also a number of possible, practical shortcomings of advance directives for dementia research.

1. A first problem is that probably few people will actually complete an advance directive for dementia research.¹⁹ Empirical research consistently shows that a relatively small percentage of people complete advance directives on future medical care, even after being informed and educated about this possibility.^{7 11 20-23} Because there is even less public awareness of and interest in advance directives for research - and probably even lesser interest in participating in non-therapeutic research - few persons are likely to complete these documents. Thus, the real impact of advance directives for dementia research should not be overestimated. This may raise serious problems when trying to recruit sufficient research subjects for specific dementia research protocols.

2. A second shortcoming precisely concerns the recruitment of persons with advance directives for dementia research. Given the fact that not many, if any, people when they are healthy, will issue advance directives for research participation, to elicit such advance directives means that it will be necessary to discuss this possibility with dementing patients in the *early phase* of their illness. However, many dementing persons go unidentified until their symptoms and problems already have reached a certain level of severity. This means that there will be a growing need for early

detection and diagnosis of dementia. Early diagnosis and screening for dementia is not morally neutral and raises in itself a number of moral issues which cannot be addressed in this paper. One issue that can be mentioned is the issue of disclosure of the diagnosis.

3. But even if it were possible to identify people suffering from dementia at an early stage of their illness, we still are faced with a third problem. This problem concerns the issue of competence or decision-making capacity. In general there ought to be a presumption in favour of considering people competent to make decisions that ought to be respected. This general presumption applies in treatment contexts, but, in my view, is less obvious in research contexts, particularly in the context of research involving no promise of benefit to the participating subject, and even more so if more than minimal risks and/or burdens are involved.¹⁹ Arguing from a decision-relative ethical perspective with regard to the assessment of decision-making capacity,²⁴ it can be argued that in order to give valid advance consent for participating in future non-therapeutic research involving more than minimal risks or burdens, a high level of decision-making capacity is needed. It is questionable whether persons in the early phase of dementia will generally satisfy such a demanding criterion.

4. A last practical problem with advance directives for dementia research is that it will be difficult to formulate wishes in terms that are neither too vague nor too restrictive.⁵ Since the directives are meant to apply in the event of future incompetence, the person formulating them now is obliged to anticipate the future and to express research wishes in the light of present knowledge, present circumstances, and fallible predictions about the course which the future will take. In different respects, there will be gaps between what was anticipated and what actually prevails. These gaps will not always be bridged by advance research directives.

Role of proxies

Because of these and other considerations the role of proxies in the context of decision-making on behalf of incompetent patients is very important. A trusted proxy of the patient may play a significant role in the decision-making process regarding the involvement of a demented patient in a particular research protocol. This role has several elements:

1. The proxy may discuss an advance directive for research with the dementing person.
2. The proxy can be consulted by the researcher,

for instance with regard to the interpretation of the advance directive, or in cases where new, unanticipated information becomes available. In both cases, the proxy should be able to use the patient's values and prior preferences as guidance for decision-making.

3. The proxy may act as a "monitor" of the research process, and may signal problems with regard to the participation of the patient in a research project.

However, the role of proxies as substitute decision-makers for dementing patients is not uncontested. Empirical research shows that proxies of dementing patients may have different views with regard to research participation than the patients for which they speak.¹¹ A more principled objection to the role of proxies as substitute decision-makers in the context of dementia research involving no potential benefits for the participating dementing person is that proxies have the duty to act in the best interests - or at least not against the best interests - of the patient. In the case of non-therapeutic research involving more than minimal risks and/or burdens for the subject it is obvious that the consent of a proxy of the patient cannot be considered to be in the best interests of that patient. This undermines the moral authority of the proxy to give consent to the participation of an incompetent demented subject in this type of research. The proxy may, however, have a significant role in giving consent for therapeutic research or in non-therapeutic research with no more than minimal burdens and/or risks.

Conclusion

In my view, the enthusiasm connected to the use of advance directives in the context of dementia research needs to be tempered. Upon a closer look, advance directives for research, particularly research involving no promise of benefit for the participating dementia patient and involving more than minimal burdens and/or risks to that patient, raise a number of moral and other problems that clearly diminish their initial attractiveness. This may also hold for advance directives in research other than dementia, but space does not permit a more extensive discussion of other areas.

Formal advance directives for dementia research can be useful and valid as supplements to current practices of proxy consent and subject assent²³ in many countries, with regard to therapeutic research and non-therapeutic research involving no more than minimal risks and/or burdens to the subject. However, on moral as well as practical grounds it is doubtful whether advance directives for dementia research can

operate as an alternative in the absence of actual subject consent in cases of non-therapeutic research involving more than minimal risks and/or burdens for the incompetent demented subject. In this context, the possible role of proxies as providers of substitute consent is also limited.

This implies that there are limits to the conduct of dementia research involving no possible benefits to the subject and with more than minimal risks and/or burdens in cases where the demented person cannot him - or herself - give actual valid consent to participate. Here I think the famous words of the philosopher Hans Jonas are to be remembered. Referring to the value and pace of scientific progress in medicine he stated:

"Let us not forget that progress is an optional goal, not an unconditional commitment, and that its tempo in particular, compulsive as it may become, has nothing sacred about it."²⁵

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